TB Elimination

# Treatment Options for Latent Tuberculosis Infection

## Introduction

Treatment of latent tuberculosis infection (LTBI) substantially reduces the risk that infection will progress to disease. Once the diagnosis of LTBI has been made, health care providers must choose the most appropriate and effective treatment regimen.

## Pretreatment Evaluation

To decide whether an individual who has a positive tuberculin skin test (TST) or blood test (QuantiFERON® -TB) result is a candidate for treatment of LTBI

- Determine the benefits of treatment by evaluating individual's risk for developing TB disease
- Assess the person's level of commitment to completion of treatment and resources available to ensure adherence

Once the decision is made to treat an individual for LTBI, the health care provider must establish rapport with the patient and

- Discuss risks and benefits of treatment
- Review possible medication side effects or drug interactions
- Emphasize importance of adherence
- Identify potential barriers to adherence
- Establish a plan to ensure adherence

## Choosing the Most Effective Regimen

Treatment of LTBI should be initiated after the possibility of TB disease has been excluded. The three treatment regimens use isoniazid (INH) or rifampin (RIF) (see Table 1). *INH for 9 months is the preferred regimen.* Treatment must be modified if the patient is a contact of an individual with INH or multidrug-resistant TB. Consultation with a TB expert is advised when the index patient has multidrug resistant TB.

### Table 1. LTBI Treatment Regimens

| Drugs/Regimen | Interval | Minimum # of doses for treatment completion | Rating for HIV-negative persons | Rating for HIV-positive persons |
|---|---|---|---|---|
| Isoniazid/ 9 month | Daily | 270 | A (II) | A (II) |
| | Twice weekly | 76 | B (II) | B (II) |
| Isoniazid/ 6 month | Daily | 180 | B (I) | C (I) |
| | Twice weekly | 52 | B (II) | C (II) |
| Rifampin/ 4 month | Daily | 120 | B (II) | B (III) |
| Rifampin and Pyrazinamide/ 2 month | Due to the reports of severe liver injury and deaths, the combination of rifampin and pyrazinamide should generally not be offered for the treatment of LTBI. | | D (II) | D (II) |

Using the U.S. Public Health Service system, CDC and ATS have ranked these regimens according to the strength of the recommendation and the quality of supporting evidence

* Strength of recommendation: A = preferred; B = acceptable alternative; C = offer when A and B cannot be given; D = should generally not be offered

† Quality of supporting evidence: I = randomized clinical trial data; II = data from clinical trials that are not randomized or were conducted in other populations; III = expert opinion

## Monitoring During Treatment

Baseline and routine laboratory monitoring during treatment of LTBI are indicated only when there is a history of liver disease, HIV infection, pregnancy (or within 3 months post delivery), or regular alcohol use. Baseline hepatic measurements of serum AST, ALT, and bilirubin are used in the situations mentioned above and to evaluate symptoms of hepatotoxicity.

Clinical monitoring, including a brief physical examination, should occur at monthly visits to assess adherence and identify signs or symptoms of adverse drug reactions.

## Drug-Drug Interactions

Obtain a list of patient's current medications to avoid drug interactions. Some interactions to note:

- INH increases blood levels of phenytoin (Dilantin) and disulfiram (Antabuse)
- Rifampin decreases blood levels of many drugs including oral contraceptives, warfarin, sulfonureas, and methadone
- Rifampin is contraindicated in HIV-infected individuals being treated with protease inhibitors (PIs) and most nonnucleoside reverse transcriptase inhibitors (NNRTIs)

## Side Effects

Patients on treatment for LTBI should be instructed to report any potential medication side effects to their health care provider, including

- Unexplained anorexia, nausea or vomiting, dark urine*, or icterus
- Persistent paresthesia of hands or feet
- Persistent weakness, fatigue, fever, or abdominal tenderness
- Easy bruising or bleeding

*Advise patients taking RIF that they will notice a normal orange discoloration of body fluids. Contact lenses may be permanently stained.

## References


ATS/CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49 (No. RR- 6). http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm

ATS/CDC. Update: Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection. *MMWR* 2003; 52 (No. 31). http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm

ATS/CDC. Treatment of tuberculosis. *MMWR* 2003;52 (No. RR-11). http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm

CDC. Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or non-nucleoside reverse transcriptase inhibitors. MMWR 2004; 53(2):37 http://www.cdc.gov/nchstp/tb/tb_hiv_drugs/toc.htm


## Additional Resources

**Website:**

TB Education and Training Resources website: http://www.findtbresources.org

The following resources can be viewed and downloaded from the CDC website at http://www.cdc.gov/tb.

**Slide Set:**

- Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection: Applying Current Guidelines in Your Clinical Practice

**Fact Sheets**:

- Treatment of Latent Tuberculosis Infection: Maximizing Adherence
- Targeted Tuberculin Testing and Interpreting Tuberculin Skin Test Results